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HUMAN TRYPANOSOMIASIS (SLEEPING SICKNESS)

in the Bolobo District of Belgian Congo.

Thesis for the Degree of M.D. 1915.

by

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INTRODUCTORY AND EXPLANATORY. (See Map.)

Bolobo is a collection of villages situated about 2° south of the equator, it is on the left, or Belgian, bank of the Congo, about 500 miles from the mouth of the river. The estimated native population is about 2,000. The population was much larger 35 years ago. At that time it was estimated at from 30 to 50 thousand, probably 50 thousand was a generous estimate. The causes of this enormous decrease of population are numerous, but one of the most important is Sleeping Sickness.

In this Thesis it is proposed to deal with the clinical aspects of Trypanosomiasis, and its treatment, in the light of the experience gained at Bolobo from 1911-1914, during which period about 600 cases were treated.

The Epidemiology, Aetiology, morbid Anatomy and Histopathology of the disease will be omitted. Only a passing reference to the History and Geography of the malady in the Bolobo district will be made. These omissions are made to reduce the bulk of the thesis, and also because the author has not had the opportunity to make a special study of these branches of the subject.

Definition of the Disease.

Trypanosomiasis at Bolobo is a chronic specific infection/

infection caused by *Trypanosoma Gambiense* (Dutton 1902) and disseminated chiefly by *Glossina Palpalis* (Robineau-Desvoidy), and characterised by an inflammatory condition of the lymphatic system leading to meningo-encephalitis and meningo-myelitis.

(Adapted from Castellani's Manual of Tropical Medicine 1913).

History and Beliefs Gathered from the Natives.

So far as one can gather from the natives, the disease has been endemic in the Bolobo district for many years. The oldest natives admit knowledge of its presence in their youth. It seems, however, that it is only within the last 15 or 20 years that the disease has caused such serious mortality.

It is believed by some natives that the floating grass islands, which are numerous when the river is rising, bring the disease. In this connexion it is interesting to note that tse-tse flies are more numerous in the villages in the high water season, than during the period when the river is low.

Natives believe that the disease is contagious. They are careful not to use the same drinking vessel, or cooking pot as an infected person. This belief has probably arisen from the fact that the disease often attacks husband and wife, and sometimes a family. There is, however, no proof to substantiate the native theory of contagion.

The/

The natives have some methods of treatment for the disease. The treatment is expensive and tedious and, so far as I have seen, worthless. Natives, however assert that they know of cases, cured, by their own doctors. There are several diseases which to the uneducated native might appear to resemble sleeping-sickness, and it is probably some of these diseases that have recovered under native treatment.

Distribution of the Disease in the District. (See Map)

The disease is widespread over the Bolobo district. In a single examination of the whole population of Bolobo in 1913, it was found that 5% of the population was infected with trypanosomiasis. It is interesting to note that the more civilized natives, who live in a colony behind the Mission Station, about 300 metres from the river, were relatively less infected than the other natives who live on the river bank, and are less protected by clothes. Only 1.5% of the population of the colony was infected.

A large number of natives from up and down river, others from the French side of the river and many from in-land (between the river and Lake Leopold II) have been treated at Bolobo.

During 1914, 290 cases were treated, these were distributed as follows.

Bolobo/

4.

Bolobo towns	88 cases	30.3%
French side	52 "	18.0%
Inland towns	42 "	14.5%
Up and down river (Belgian side)	<u>108</u> "	<u>37.2%</u>
	<u>290 cases</u>	<u>100.0%</u>

Only the Bolobo towns were systematically examined for sleeping sickness.

Influence of Age and Sex.

An analysis of 600 cases of trypanosomiasis treated at Bolobo demonstrates that there were approximately twice as many males as females treated. (66% males, 34% females). This result agrees with Todd's figures for Congo in 1903-1905. (see table 2), and also with the observations of Sanderson (1912) and Hearsey (1912) in Nyasaland.

Scott Macfie (Annals of Tropical Medicine Vol.8 page 388) gives a graph representing the age incidence of 222 cases seen in the 'Eket' district of Southern Nigeria. This graph is reproduced under the graph representing the age incidence of the 600 Bolobo cases. (Chart 1). It will be seen that the disease attacks very young people in Nigeria more frequently than at Bolobo, and also that middle-aged people are more frequently infected at Bolobo than in the 'Eket' district.

Todd suggested that the influence of sex and age should be considered by enumerating the cases occurring in children, adults, and old people, of the two sexes. He considered that male children take upon themselves the occupation of adults at the age of 14, and female children at the age of 12. Elderly people he regarded as those over 45 years. This suggestion has been adopted, and tables 1 and 2 show the result of such an analysis of our cases, and compares it with Todd's figures./

figures.

Considering how difficult it is to determine the age of a native, it is remarkable that the results of an analysis should so nearly agree with those obtained by Todd in Congo 1903-1905. The one great discrepancy is that the number of male children in our figures is much larger than the number given by Todd for Congo in 1903-1905. The number of female children is also larger in our figures. These differences may be due to the fact that our observations are spread over a longer period than those of Todd. It is necessary to stay some long time in a native town before one can examine the whole population in anything approaching a thorough manner.

Chart 1.
 Showing age incidence of 600 Batido cases of trypanosomiasis
 compared with McTig's 222 cases at Blit.
 (Shaded in period of 5 years).

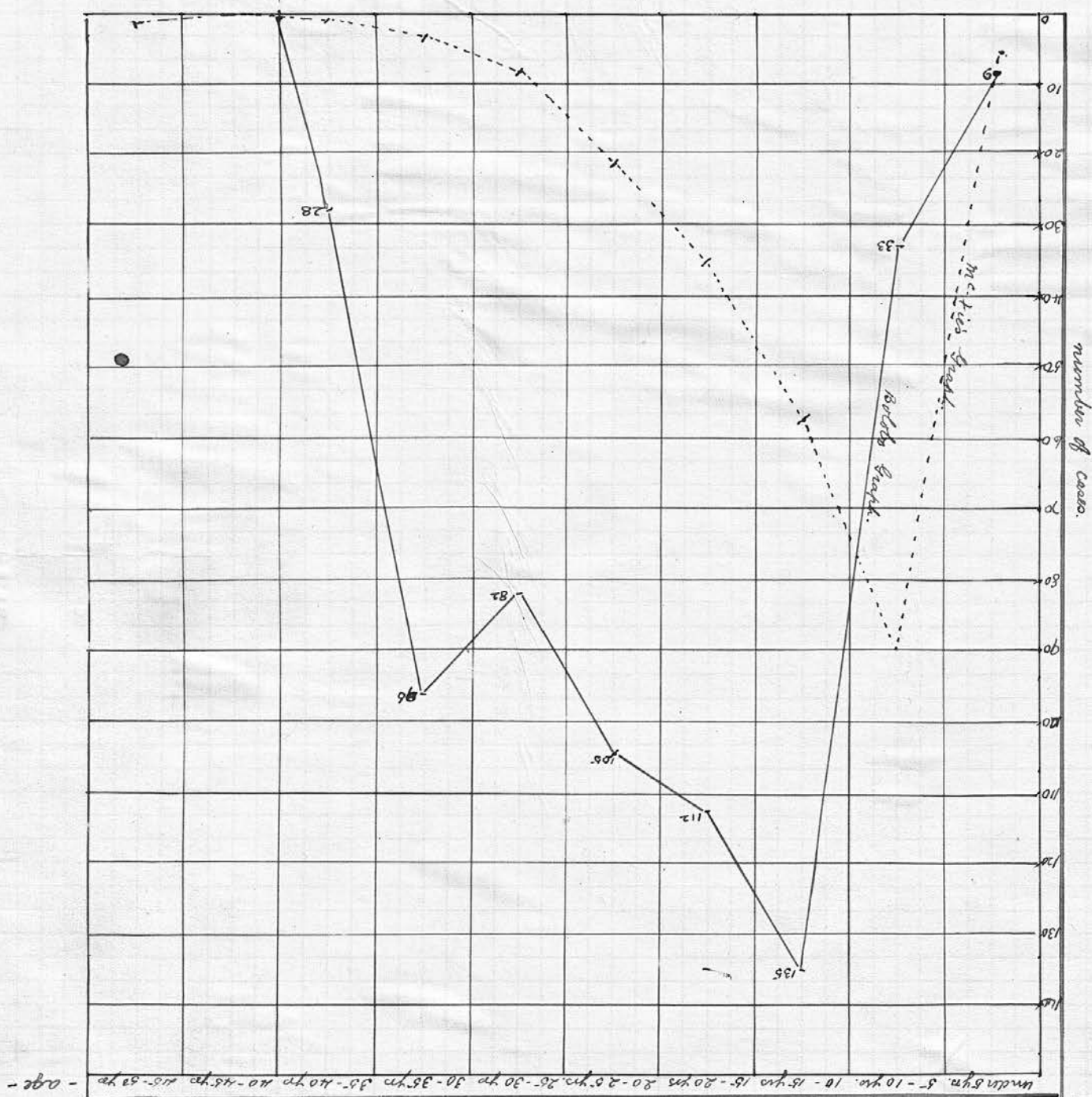


Table 1. Age and Sex.

Analysis of Bolobo cases of trypanosomiasis compared with Todd's figures for Congo and Gambia.

	Males.			Females.			Totals.	
	0-13	14-44	45+	0-11	12-39	40 +	%	Cases.
Congo 1903-1905 Unselected population. (Todd)	6.1%	57.2%	2.0%	2.0%	32.7%	0.0%	100%	147
Congo 1903-1905. Selected population. (Todd)	6.7%	63.2%	0.7%	2.6%	26.8%	0.0%	100%	269
Gambia 1911 Todd.	16.4%	39.3%	0.0%	7.6%	36.7%	0.0%	100%	79
Bolobo 1911-1914.	16.0%	50.0%	0.0%	5.3%	28.7%	0.0%	100%	600

Table 2.

	Age (both Sexes)			Sex (all ages)	
	Children	Adults	Aged	Males	Females.
Congo 1903-1905. Combined populations.	8.7%	89.95%	.35%	67.95%	32.05%
Gambia 1911.	24.0%	76.0%	0.0%	55.7%	44.3%
Bolobo 1911-1914.	21.3%	78.7%	0.0%	66.0%	34.0%

SYMPTOMATOLOGY.

It is convenient to follow Castellani's division of the course of the disease into three stages.

1. The Incubation stage
2. The Febrile or glandular stage
3. The Cerebral stage.

1. The Incubation Stage.

It is extremely difficult to estimate the length of this stage from cases occurring in black patients, because one is unable to fix either the date of infection or ^{of} the commencement of the disease.

The bite of the *Glossina palpalis* is frequently painful to a white man, but it seems to affect a native very slightly, and is easily passed over without notice.

In four white patients, suffering from trypanosomiasis, that I have seen, the incubation period seemed to be under three weeks. Two had only been a short time (about 3 weeks) in the country when they began to suffer from irregular fever, which was probably the commencement of trypanosomiasis fever. One other was bitten by a fly three weeks before the onset of the fever, the bite was very painful, and gave rise to local swelling. The fourth had been exposed to the bites of several flies on the river about three weeks or so before the onset of his fever; he had no idea of the day on which he might say he had been infected.

Cases of very long incubation periods of one year and over have been described by some observers. It seems/

seems possible that these are rather cases where the febrile stage has been very prolonged and mild, and the attention of the patient was not drawn to his condition by any symptoms until he had been a subject of the disease for many months.

Castellani puts the usual incubation period at under two or three weeks.

2. Febrile or Glandular Stage.

In our cases the symptoms of this stage in natives were often absent until the border line of the cerebral stage had been reached. In some natives, however, and in all white patients, the symptoms described below were well marked.

Fever.

The fever of trypanosomiasis is in the majority of cases the first clinical symptom. The typical trypanosomiasis fever shows irregular intermissions. The fever is usually remittent in type. The evening temperature rises to 100° - 101° or even 102° , and the morning temperature is usually about 99° or 99.4° . Sometimes there are no periods of intermissions, and the fever is continuous.

Pulse.

The pulse rate is increased during the fever, and often remains quick when the temperature falls. It is extremely rare that one finds a slow pulse in this disease./

disease. The pulse tension is usually low.

Skin Rash, etc.

The rash which accompanies trypanosomiasis is an erythematous eruption. Patches of erythema are seen most frequently on the chest or back, rarely on the limbs. These patches usually clear in the centre and thus present the appearance of reddish rings, often slightly raised. The majority of black patients did not show any definite rash, but it was seen in a few cases. It was present in all the European cases seen.

A papular rash has been described as occurring in some patients. A number of our patients certainly presented a papular rash, but it was proved to be an intercurrent skin disease to which sleeping sickness patients are especially prone; namely scabies.

The skin of the native affected with trypanosomiasis quickly loses its glossy character, and becomes dry and greyish, and shows a tendency to desquamation.

Sometimes patches of oedema are seen at this stage. Oedema of the eyelids, face and hands have been noticed. This symptom, however, is much more common in the next stage of the disease.

Enlargement of Lymphatic Glands.

This is the most important symptom of the first stage of trypanosomiasis from a diagnostic point of view. The glands of the posterior triangle of the neck are most constantly affected. It is also usual to/

to find other lymphatic glands enlarged, especially the submaxillary and supraclavicular groups, and the epitrochlear glands. The glandular enlargement does not often cause pain or inconvenience, but sometimes pain or stiffness of the neck has been complained of.

The glands vary in size, from the size of a hazel nut to the size of a walnut; they are ovoid in shape and soft and elastic on palpation. A number of natives have the glands of the neck enlarged quite apart from sleeping sickness. Our experience has been that from 10 - 15% of natives with enlarged glands are infected with the disease.

A few cases have no marked glandular enlargement.

The glands become sclerosed and diminish in size as the disease advances.

The spleen is usually enlarged, but it is difficult to say whether this enlargement is due to malaria or sleeping sickness.

Other Symptoms Noted.

Headache, backache and general weakness are often complained of, and are practically always present in Europeans. Loss of appetite is frequent. Anaemia may be marked and is almost always present in some degree.

Amenorrhoea in the female, and impotence in the male were among the most frequent symptoms that brought infected natives to us for advice, usually however these/

these patients were in the Cerebral stage of the disease. Amenorrhoea and impotence are sometimes early symptoms in the disease.

Deep hyperaesthesia (Kerandel's symptom) was only present in a small proportion of our cases.

The duration of the febrile stage is variable. It may only last for a few months or it may be continued for a year or longer.

3. The Cerebral Stage.

The cerebral stage is extremely variable, both in relation to the symptoms manifested, and to the length of the course it may run.

Appearance of the patient.

There is usually a marked change in the appearance of the patient. This is so much the case that it is often possible to diagnose trypanosomiasis with considerable accuracy, in this stage, from the general appearance of the patient. The face is usually puffy, giving an idea of unhealthy plumpness. The eyes are bleared and dull, there is a lack of expression about the face. The whole body of the patient may present the same swollen appearance as the face, but sometimes there is extreme emaciation. The skin loses its glossy appearance and is paler than normal, and very frequently there is some eczema or impetigo or scabies about the body, especially around the buttocks and legs. The hair is usually less curly, and less glossy and often/

often it is of a brownish colour, and less in quantity. There are marked tremors of the tongue, and often tremors of the hands and feet. The patient is usually dirty in appearance and in his habits.

Gait.

The gait of the sleeping sickness patient is usually of a slow shuffling type. He does not lift his feet well. Sometimes the gait is affected by the enormous number of chiggers these patients frequently have in their feet.

Mental and Moral changes.

The disposition and character of these patients often undergo a change as the cerebral stage of the disease grips them. An industrious and trustworthy workman may become lazy and dishonest. Often the moral character of the patient is entirely changed. It is necessary to bear this in mind when dealing with misconduct in natives of previously good character.

Many of these cases become quite insane. Acute mania, Kleptomania, Pyromania, moral insanity, melancholia, and other forms of mental disease have been noted frequently among our cases. One case of puerperal insanity was afterwards proved to be a case of trypanosomiasis.

Cases of epileptiform seizures are not uncommon. In one of these cases the fits lasted for 12 hours and on recovery he was found to have hemiplegia.

A certain percentage of the patients follow the classical description of Sleeping-sickness and become lethargic. Most of the patients sleep more than normal people, some are rarely awake, and are found asleep in quaint positions and in curious places. One patient slept soundly in the open through a severe tornado which failed to waken him. It is interesting to note that patients may live several weeks or even some months in a semi-comatose condition, and with very little nourishment.

Other Symptoms.

Nearly all complain of severe headaches, backache, and great weakness. Natives frequently complain that their "eyes turn round" which probably denotes giddiness. The appetite is often enormous, but sometimes it is impaired.

Amenorrhoea and impotence are constant in this stage. This is a well recognised danger signal among the natives, and it is well to exclude sleeping sickness in all cases of this nature. In a few cases insomnia has been a very troublesome symptom.

High fever is frequent among these patients, and the pulse rate is usually well above 100° up to 140°. The respirations are quickened, and towards the end Cheyne-Stokes's breathing may be noted. There are sometimes systolic murmurs to be heard over the pulmonary area. The red blood cells are usually markedly/

markedly diminished in number, sometimes as low as 2,000,000. There is usually no leucocytosis.

The red blood cells do not tend to form rouleaux to the same extent as in normal blood, but are seen in clumps in the blood film. Opinions differ as to the value of this phenomenon in the diagnosis of the disease.

The glands of the neck undergo fibrosis and are often very small in this stage of the disease.

The deep reflexes are at first exaggerated and then later they are usually lost.

Romberg's sign is sometimes present, but by no means constant. Sometimes inco-ordination of movement is seen.

As the disease advances the patient is confined to bed, and becomes emaciated and extremely weak. Control of the bladder and rectum is lost. Congestion and oedema of the lungs is apt to occur. Tremors are more pronounced. Saliva dribbles from the mouth. Rigidity of the muscles of the neck and legs and abdomen appears. The legs are kept in the flexed position. The pulse becomes imperceptible at the wrist. Bed-sores are very apt to appear, and hasten the end of the patient.

The duration of this stage of the disease is variable, if untreated usually a few months is probably the longest a patient will live, but we have had cases live for two years in this stage while under treatment.

COMPLICATIONS.

The commonest complications noticed at Bolobo are dysentery, and intestinal parasites. Ankylostomes are extremely common, and *Ascaris lumbricoides*, and *Trichocephalus dispar*, have been found in nearly all the cases.

Pneumonia has carried off a number of our patients.

Scabies, impetigo are very frequent in the cerebral stage, due largely to the filthy condition of the patient.

Chiggers and vermin worry the patient.

Hemiplegia has been noted in three cases. Spastic Paraplegia in two cases.

DIAGNOSIS.

It is important that a diagnosis should be made in the first stage of the disease if possible, because it is only in early cases that there is a reasonable hope of carrying out a successful treatment.

The fever of trypanosomiasis is as a rule only of diagnostic value in European patients, as natives rarely seek medical advice for fever. A continued fever, or several severe attacks of fever will, however, sometimes bring a native to the doctor. The important point of distinction between malarial fever, and trypanosomiasis fever, is that the latter does not respond to quinine. In an endemic area, all fevers that do not respond/

respond to active treatment with Quinine should lead one to think of trypanosomiasis.

In an apyrexial period, the rapid pulse may sometimes be of diagnostic value. The rash is helpful in Europeans and rarely in natives. Fine tremors of the tongue, deep hyperaesthesia are of a certain diagnostic value.

The most important symptom of the first stage is enlargement of the cervical glands. It is useful to accustom oneself to the feeling of typical trypanosomiasis glands, as their shape and consistency are wonderfully constant in infected patients. ("Boules élastiques" Stohr.)

The only certain method of determining a diagnosis is to isolate the trypanosome by one of the methods given below.

In the second stage of the disease the symptoms are so marked, and the general appearance of the patient is so typical that diagnosis is usually easy. It is necessary, however, to isolate the trypanosome in all cases to be absolutely certain of a diagnosis.

Symptoms of insanity, epilepsy, amenorrhoea, impotence, progressive weakness, irregular fever, and somnolence should be regarded with suspicion, and sleeping-sickness should be excluded by searching for the trypanosome.

Methods employed for searching for trypanosomes.

The/

The methods given are placed in the order of their clinical value.

1. By gland puncture.

This method is known as the Greig-Grey method, and was first suggested by Mott. It is by far the most satisfactory of methods.

A platinum-iridium hypodermic needle is the best instrument to use, as it can be sterilized in the flame of a spirit lamp. The needle must be dry as well as sterile. Trypanosomes are sometimes very numerous in gland juice. We have seen three and four in one field with a one-sixth inch objective, usually, however, they are not very numerous, and a careful search is necessary. We search for at least 15 minutes, and if the result is negative, our further procedure depends on the condition of the patient. If he presents symptoms of trypanosomiasis apart from his glandular enlargement, he is asked to submit to the puncture of another gland. If this is again negative we centrifuge 10 c.c. of his blood in the method described below. If no other symptoms of trypanosomiasis are present, and the gland puncture yields a negative result, he is considered free of trypanosomes, and is asked to return should he suffer from fever or other symptoms of the disease.

2. Repeated Centrifugation of 10 c.c. of blood (Nabarro)

If the gland puncture is negative, and it is desired to carry the investigation further, we proceed as follows.

- (1) Into a 10 c.c. syringe draw up 1 c.c. of 10% Sodium Citrate solution.
- (2) Into this same syringe draw up 9 c.c. of blood from a vein in the arm - mix well.
- (3) Centrifuge this citrated blood gently for about 10 minutes until the corpuscles have well separated from the serum.
- (4) Draw off the serum and centrifuge it for another 10 minutes.
- (5) Again draw off the serum and centrifuge it vigorously for 20 minutes.
- (6) Examine the deposit for trypanosomes.

In a few cases we have been successful in finding trypanosomes by this method, when gland puncture has failed to reveal their presence. The objections to the method are that it is tedious, and also disagreeable to the patient. It is useful when the glands are small or fibrosed.

3. Examination of fresh blood films.

This method is useful in white patients. For some unexplained reasons it is the experience of several observers in Belgian Congo that it is more difficult to find the trypanosomes in blood films taken from the thumb or ear of infected natives than that taken from infected Europeans. In 1908-1909 this was the only method employed at Bolobo and in only 2% of suspected cases were trypanosomes discovered. Even in white patients gland puncture is much more certain.

4. Examination of the Cerebro-spinal fluid.

About 10 c.c. of cerebro-spinal fluid is withdrawn by/

by lumbar puncture, and centrifuged for about 15 minutes. The sediment is examined for trypanosomes. The result is only positive in the second stage of the disease. The cellular elements of the cerebro-spinal fluid should be examined; if a large number of mono-nuclear leucocytes are present in a person known to be infected with trypanosomes, the prognosis is grave. A turbidity of the cerebro spinal fluid is also a grave sign.

If all the above mentioned means fail to reveal trypanosomes in a patient with typical symptoms, the diagnosis is difficult. It is better to regard such a case as trypanosomiasis and treat it as such. If possible, it is well to inoculate a susceptible animal with some blood of the patient. At Bolobo we had no animals for this purpose.

F. O. Stohr in "La maladie de sommeil au Katanga" says in reference to these cases that have typical glands and other symptoms:

"In such a case, even if a puncture (of the gland) does not reveal a trypanosome, I would not hesitate, in reckoning my statistics, to count him among those infected, unless the glandular enlargement was explicable by some other cause."

He continues

"I call "probables" the cases in which the glands are swollen but less characteristic, or if it is impossible to puncture them, I reckon 50% of these "probables"/

"probables" among the "contaminated."

Scott Macfie (Annals of Tropical Medicine Vol.8, page 384)

"During the 16 months in which sleeping sickness has been under investigation 222 cases have been identified in which trypanosomes have been demonstrated. In addition 114 cases have been met with presenting some of the clinical features of the disease, but in which parasites have not actually been found".

Of the 600 cases treated at Bolobo, trypanosomes were found in 528 (88%). The other 12% showed such marked clinical symptoms of the disease that they were regarded as cases of sleeping sickness.

In view of the two facts, (a) that it is of vital importance to make an early diagnosis in this disease, (b) that the symptoms experienced by natives in the early stages of the disease are frequently so slight as to be passed over, it is advisable to make periodical examination of the cervical glands of all the native population under the administration of a doctor who is engaged in sleeping sickness work. This was carried out at Bolobo in 1913 and early in 1914. Unfortunately a press of other work hindered the continuation of these systematic examinations for the last year of residence at Bolobo.

It is remarkable how many apparently perfectly healthy individuals are infected with trypanosomes, and are thus acting as reservoirs for the infection of the flies which spread the disease.

PROGNOSIS.

The prognosis is very grave for all cases that have reached the cerebral stage. Cases in the first stage of the disease are not hopeless. Six cases occurring in the last eight years in white people in Belgian Congo have come under our notice, and all are well, and apparently have made a good recovery. It is difficult to remove natives from the endemic area, and this militates against their chance of recovery, but the results of treatment given below will demonstrate that their case is not hopeless.

We have never seen a case with mental or cerebral complications make a complete recovery. The lives of these patients can be prolonged, and their condition improved, but relapses are to be expected. It is always to be remembered that some cases run a rapid course, and also that patients suffering from sleeping sickness are liable to be carried off suddenly by complications such as pneumonia and dysentery, therefore the prognosis must always be guarded.

One case is worth special notice under the heading of prognosis. A man of about 30 or 35 years was found to be infected with trypanosomes, by means of gland puncture in the Spring of 1913. He was frightened at the prospect of treatment and ran away from the district. He returned in the Autumn of 1914. On examination no trypanosomes could be found either by repeated/

repeated gland puncture or by centrifugalization of blood. He was in quite good health, and had received no treatment whatever for trypanosomiasis. The case is still under observation. The question arises, is this a case of spontaneous cure, or is it a case in which the disease is remaining latent for an unusually prolonged period. The latter is the more probable solution. From this case it is evident that it is impossible to predict the course that the first stage of trypanosomiasis will run.

It is also our experience that a large number of trypanosomes found in the gland juice has no bad effect on the prognosis. One case "Mbele" a girl of 15 is worth citing in this connection. Our attention was drawn to Mbele in May 1913 by the fact that she had enlarged glands. There was a history of frequent attacks of fever, also she had never menstruated. She was found to have an exceptionally large number of trypanosomes in her gland juice. She was treated with 25 injections of atoxyl, 5 grs. each injection, and has made so far as we can tell a good recovery. Menstruation started early in 1914. A recent letter from Bolobo, dated June 1915, tells us that she is pregnant.

Our experience has been that the number of trypanosomes found in the gland juice has no bearing on the prognosis.

TREATMENT.

An entirely satisfactory treatment for Sleeping Sickness has not yet been found. Great progress has been made in the last ten years. There are a number of trypanocidal drugs on the market, but none of these has any lasting effect upon the disease in those patients who are in the second or cerebral stage.

Patients in all stages of the disease usually improve rapidly under treatment, but relapses are common and are to be expected in the second stage of the malady. The trypanosomes quickly disappear from the cervical glands, and the glands rapidly diminish in size.

Most observers agree that the most valuable drug for the treatment of Sleeping sickness in Congo is Arsenic in the form of Atoxyl. Soamin and Arsacetin are similar in their composition and in their action to Atoxyl and can be substituted for it. The advantage possessed by Soamin and Arsacetin is that a solution of either of these drugs can be sterilized by boiling, while atoxyl decomposes at a temperature below the boiling point of water. The three drugs were used indiscriminately at Bolobo and formed the basis of treatment for practically all the cases.

Salvarsan, and Neo Salvarsan have been used, and are of advantage when one cannot see the patient frequently, as it is not necessary to repeat the dose for some weeks, or even three months. The drug, however, /

however, is expensive and seems to have no more specific action on the disease than Atoxyl.

Liquor arsenicalis was used before the introduction of atoxyl, and is still useful in cases where for some reason injections cannot be made. It should be given in doses of 5 minims three times a day, and the dose increased by 1 minim each day, till the patient is taking 15 minims three times a day, then it may be decreased again until 5 minims a day is reached. After such a course the patient should be allowed a rest of a week or so before again commencing treatment. The difficulties of the treatment are that the natives do not take medicine systematically for a long period unless they are supervised, and that arsenical poisoning and Gastritis are likely to occur.

Dutton and Todd visited Bolobo in 1905 or 1906, and discovered some cases of trypanosomiasis (number of cases unknown). These patients were treated by the above method with Liquor arsenicalis. Two are still alive; one, "Molonzombo", suffers from periodical attacks of insanity, while the other, "Liloko", is in good health. The latter so far as one can gather from his own history was only in a very early stage of the disease when diagnosed. These two cases tend to prove that Liquor Arsenicalis may have beneficial effect on some cases of trypanosomiasis.

Orpiment, we have used latterly for cases who have completed their course of Atoxyl injections. It is still/

still too early to decide whether any benefit was gained. Orpiment has proved of value in conjunction with Atóxyl and is recommended by Laveran and Thiroux.

After Arsenic, the next most valuable drug is Antimony. At the Government Laboratory at Leopoldville, tartar emetic is given as a routine treatment in conjunction with Atoxyl. The usual dose is $1\frac{1}{2}$ grs. of tartar emetic in 1% aqueous solution. This solution is injected into a vein, once a week.

Mercury in the form of Corrosive sublimate is being tried at Bolobo. Dr Gamble of San Salvador recommended this treatment in an article published in the Journal of Tropical Medicine and Hygiene. It is difficult to say whether the results will prove successful at Bolobo.

By the courtesy of Dr Vandenbranden I have a copy of the report of the Laboratory and Lazaret at Leopoldville, Belgian Congo, 1914, which gives a list of drugs that have been tried during the year. Trypanblan, Trixidine (oily emulsion of the trioxide of Antimony), Thiarsol (Isotonic colloidal sulphide of Arsenic As_2S_3), Trypanosan I and II of Krause (bodies of the series of Triphenylmethane), Salicylate of Soda associated with Salvarsan. All these except the last, were of no use against the disease, and some were described as dangerous. The last (Salicylate of Soda and Salvarsan) was suggested by Morgenoth and did not show any special advantage in the second period of the disease.

Kupfersalvarsan (Ehrlich) and Kupfersalvarsan Natrium (Ehrlich) seem to be of some value, and the report/

report is worth quoting.

"(1) Kupfersalvarsan. (P. Ehrlich).

Combination of copper and salvarsan. The experiments undertaken in 1913 have been continued. Kupfersalvarsan has given us sterilizations of long duration, perhaps some definite cures, among trypanosomiasis patients of the first period of the malady.

Thus "Mandunga" whose blood has remained sterile 18 months after two injections of 0.1 gramme; "Luyeye" sterile 18 months after one injection of 0.2 grammes. "Kissuna" who does not present any relapse 18 months after one injection of 0.1 gramme. "Libengo" sterile 17 months after one injection of 0.3 gramme, and other observations which we do not mention here.

On the other hand we have had some rapid relapses (25 days - 1 month) as much among those patients of the first period as among those who had the spinal fluid changed (*altéré*).

The strongest dose given was of 0.005 gramme per kilo. of body weight; this is a dose which must not be surpassed. One can give with impunity a series of 6 or 8 injections of 0.1 gramme.

Just like Salvarsan and Neosalvarsan, Kupfersalvarsan has no favourable action on those who have their spinal fluid altered."

(2) "Kupfersalvarsan Natrium (Ehrlich) The soda salt of Kupfersalvarsan. Employed on the instructions of Professor Ehrlich in a series of 6 or 8 injections of 0.1/

0.1 gramme and 0.15 gramme, this treatment (médicament) has given bad results.

Single doses of 0.3 gramme and 0.4 grammes seem to give better results. The time of observation of the patients being too short, we cannot at this moment pronounce a verdict on its value. It seems to us, up to the present, that it is called to surpass Kupfersalvarsan by its more rapid and practical mode of administration (son emploi plus rapide and pratique)!"

Treatment and Results at Bolobo.

From January 1911 to March 1912, 64 patients were treated. The treatment followed was the injection into the muscle of the buttock of 3 grains of Atoxyl dissolved in 20 minims of water. The treatment was repeated 3 times a week, for 8 or 9 weeks. Three grains was taken as the dose suitable for an adult of 140 lbs weight, and the dose was reduced for small adults and children. The only other treatment followed at this time was to give an alkaline tonic containing Tinctura Nucis Vomicae. The results were not very encouraging. Only 50 of the 64 treated were traced; one of these 43 (86%) were dead by March 1915. The average length of life of those who died was 18 months, and the longest period that elapsed before death was 42 months, and the shortest 4 months. Five are still alive and well; in all these five trypanosomes had been identified before treatment. Two of these five were/

were women, and both have given birth to healthy children. Two were men and both are doing their ordinary work. The fifth was a boy of ten at the time of treatment. The remaining two patients are alive, but in an unsatisfactory condition. They have both suffered from repeated relapses, and are unlikely to live long.

From March 1912 to April 1913 we used 5 grains of Atoxyl injected into the buttocks twice a week, and once a week we injected $1\frac{1}{2}$ grains of tartar emetic in 1% aqueous solution into a vein of the arm. The results obtained during this period were much better, firstly because a larger percentage of the cases were in the first period of the disease and secondly because the treatment was carried out more actively and more regularly. 115 patients were treated during this period and of these only 84 were traced in March 1915. 42 (50%) of these had died, and 32 were alive and healthy. 10 were in an unsatisfactory condition from relapses.

This treatment is probably the most satisfactory for Congo trypanosomiasis. The Antimony was given up at Bolobo because we wished to discover whether it was affecting the results, and also because the injection is troublesome. The smallest leakage of the solution into the tissues round the vein gives rise to very severe and painful irritation and swelling. Some patients/

patients complained of pain after the injection, and others were attacked with vomiting and coughing. For these reasons it was found difficult to persuade the patients to undergo this treatment. Our natives are nervous and easily frightened. In young plump black children it is very difficult to find a vein with the needle. The advisability of recommencing the intravenous injection of tartar emetic will be seriously considered when the Sleeping sickness work is resumed at Bolobo.

From April 1913 to March 1914 Atoxyl was given in 5 grain injections three times a week, and no other treatment was superadded. The cases are still being watched. 198 were treated, of which only 110 could be traced. Of these 110, 24 had died before March 1915, and 26 were in an unsatisfactory condition. 60 were in a good state of health, so far as one could tell.

In March 1914, we commenced the administration of corrosive sublimate by mouth. In addition to the Atoxyl treatment 30mm. of the Liquor Hydrargyri perchloridi was given three times a day by mouth. It is too early to say whether this treatment will have any better results, but of the 223 patients treated during this period 106 only were traced, of which 18 have died, 20 were in an unsatisfactory condition and 68 were still apparently well and had had no relapse.

These results are tabulated in Table III.

Table III.

Shewing results of treatment of Bolobo cases and their condition in March 1915

Treatment (Adult doses given.	Date of Treat- ment.	Total No of Cases	Deaths	Unsatisfactory		Not traced	Died	Result in % of number traced.	
				factory	Healthy			Unsatisfactory	Healthy.
3 grs. of Atoxyl in- jected in- to the buttock 3 times a week for 8-9 weeks	Jany. 1911 to March 1912.	64	43	2	5	14	86%	4%	10%
5 grs. of Atoxyl in- jected in- to the buttock twice a week for 12-13 weeks, & 1½ grs of Tartar emetic in- to a vein of arm.	March 1912 to April 1913.	115	42	10	32	31	50%	12%	38%
5 grs. of Atoxyl in- jected in- to the buttock 3 times a week for 8 or 9 weeks.	April 1913 to March 1914.	198	24	26	60	88	21.8%	23.6%	54.5%
5 grs. of Atoxyl in- jected in- to the buttock 3 times a week for 8 or 9 weeks, & 30 mm. Liq. Hydrag. perchlor. t.d.s.	March 1914 to Dec. 1914.	223	18	20	68	117	17.9%	18.9%	64.1%
Totals.	1911- 1914.	600	127	58	165	250	36.3%	16.6%	47.1%

Salvarsan was tried in four cases that had relapsed after a course of treatment with atoxyl, but in none of these cases did we note any marked improvement, only one is still alive and in an unsatisfactory state.

In three cases, Salvarsan was given in the first instance. In two cases there were relapses in 3 - 6 months and in the third case the patient is alive and well 12 months after the injection.

In the Tropical Bulletin, 1914, Vol.3, No.10, Mouchet and Dubois reported that single injections of Salvarsan or of Arsenophenylglycin produce apparent cures in patients in the first stage of the disease. The experience at Bolobo of Salvarsan is so small that we cannot criticize this statement. One of our three cases certainly helps to substantiate its truth. Salvarsan is valueless in the second stage of the disease.

Our treatment for relapses is to repeat the treatment carried out in new cases. All cases in the second stage receive a second course of injections two months after the first course has been completed.

We have never had a case of blindness or other ill effects from Atoxyl.

An important question to be decided is the value of Lazaret treatment for cases of Sleeping sickness. Opinions differ. Theoretically it is advisable to isolate all infected persons in a Lazaret situated outside the fly area. In a Lazaret regular and systematic/

systematic treatment can be carried out. The difficulties to be faced are the expense of maintaining such a camp, the difficulty of sanitation and also the great difficulty of retaining the patients in the Lazaret.

To maintain a Lazaret the cost would be at Bolobo at least £6 a patient per annum for food and clothing; other expenses would be small as the administration and sanitation could largely be carried out by the stronger patients. Natives do not as a rule like to be placed in a Lazaret away from their friends, and it is necessary to keep the patients by force in the majority of cases.

At Bunkeya in the Katanga district of Belgian Congo, about 20 ran away, out of a total of 81 admissions into the Lazaret. At Leopoldville where there is an excellent Lazaret, the figures were 13 deserters out of a total admission of 210; and this can be regarded as a minimum leakage by desertion. Only 21 of the 210 were in the first period of the disease, and it is these apparently strong and healthy people that it is difficult to detain.

At Bolobo lack of the necessary funds has prevented us from undertaking extensive Lazaret treatment. We have little or no difficulty in getting patients to come regularly for their injections now. At first it was difficult, but as the successful treatment of some cases is demonstrated to the natives they become quite anxious to receive the necessary injections.

of/

Of our 600 patients the vast majority were treated as out-patients and only 36 (6%) ran away before treatment was complete.

Lazaret treatment is necessary for patients who come from a distance, but in Belgian Congo the majority of doctors prefer the ambulatory treatment for those who can attend regularly for injections.

The necessity for isolating the patient under treatment in Lazarets in order to prevent the spread of the disease is disputed by some.

It is generally held that patients receiving injections of Atoxyl are not so likely to infect flies that may bite them, as untreated cases. It has been proved by the Sleeping Sickness Commission 1913 that patients under treatment can infect flies. Out of 35 experiments of this nature, one was positive. The flies were infected 25 days after the last of a series of four injections received by the patient.

(S.S. Commission Report. No.XI, page 111.)

Dr Van Someren of Uganda says: "In my opinion Lazarets are only charitable refuges where unfortunate natives find a peaceful end in an agreeable surrounding. They cost extremely dear and are of little practical utility". (Quoted from F.O. Stohr. La Maladie de Sommeil au Katanga, page 57.)

PROPHYLAXIS./

PROPHYLAXIS.

The prophylactic treatment of Sleeping sickness necessitates a large staff of doctors, endowed with full authority by the government, and also adequate funds should be at their disposal. At present little has been done in the Middle Congo, owing to lack of funds and medical men. A complete study of the distribution of *Glossina palpalis* has not been made. This is the first necessity. That being accomplished it is necessary, either to remove the population from the fly areas or to take measures to eliminate the flies. The clearing of the villages and banks of the river of trees and undergrowth is a difficult but necessary task. This has been begun at Bolobo, but it is necessary to repeat the clearing from time to time as the bush grows again very rapidly. The effect of clearing can be seen at Bolobo. The Mission station has been kept clear for some years, and it is rare to see a tse-tse fly on the station, while in the lower villages tse-tse flies are common especially in the high water season. These villages are being cleared now.

The next important point in prophylaxis is the active treatment of all infected persons, and if possible the isolation of those infected outside the fly area. A systematic examination of the whole population should be made every three months.

All/

All infected natives should be prevented from travelling on river steamboats. It is compulsory in the Middle Congo for all native passengers and crew of steamers to have in their possession a medical passport, stating that they are free from trypanosomiasis. This passport must be signed by a doctor every three months. Unfortunately owing to the small number of doctors this system of passports breaks down.

Especial care should be taken in the examination of all persons entering an area uninfected with sleeping-sickness, from an infected area.

Reservoirs of the trypanosome should be searched for, and if it is found that wild or domestic animals harbour the organisms, these animals should be sacrificed.

In the island of Principe, De Costa was able to do a great deal of good by employing a number of natives as fly-catchers, and thus reduce the number of flies. Natives were clad in black cloth smeared with bird lime to catch the flies. Unfortunately some of these natives were infected (4 out of 120) at their employment, in spite of a prophylactic dose of Atoxyl.

White clothes and putties are a protection against tse bites, and as most Europeans in the tropics wear white it is probably one of the causes of the relative immunity of the white man from the disease.

The/

The cases given below illustrate many points mentioned.

Ebonga, male aged about 26, came in May 1911 complaining of headache, backache and impotence. He also complained of dimness of vision, but this symptom could not be substantiated by the usual clinical tests. He was thin and had had several small fevers, the glands of his neck were enlarged, and trypanosomes were found in his gland juice. He commenced injections of atoxyl, 3 grains in 20 minims of water three times a week on May 15th, 1911, and received 21 such injections into the muscle of his buttock. He was examined, by gland puncture and by centrifugalization of 10 c.c. of his blood on October 24th, 1912, and no trypanosomes could be found.

In March 1915 he was still alive and apparently healthy. He has had no relapses and the disease shows no signs of passing into the cerebral stage. He still is able to carry on his work as a carpenter, and can be regarded as a case of apparent cure. His impotence has not entirely disappeared, and he sometimes suffers from headaches. He has had one child.

Monketu, male aged 20, a compositor employed by the Missionary Society Press at Bolobo. He was complaining of headache and fever. Glands of the neck were enlarged and trypanosomes found in March 1911. He commenced injections on March 8th and received 80 grains of Atoxyl in all. His condition improved immediately/

immediately and he has remained well ever since. He was married in 1913, and his wife had one child early in 1914. The child was premature and died soon after birth. She was again pregnant in March 1915. Monketu worked as dresser in the dispensary for over a year (1913-1914) and was intelligent and industrious.

Wakake, male 35 years old. He came complaining of headache, giddiness, fever. His glands were enlarged and trypanosomes were found in June 1911. He received 64 grains of Atoxyl in 16 injections and then returned to his home inland. He remained well for three years, and then had a severe relapse and refused to return to Bolobo for treatment or examination. He died apparently from sleeping-sickness in February 1915. It would be interesting to know whether this was a case of relapse or re-infection.

Epalanza a lad of 10 came complaining of weakness, fever and headache. Trypanosomes were found in his gland juice in September 1911. He received 60 grains of atoxyl in 20 injections and returned to his village much improved. In June 1912 he was well. He returned in a much worse condition in February 1914. His appearance was that of a typical sleeping sickness patient of the cerebral stage. He was very lethargic, tremors were well marked, his gait was shuffling, his skin dull, and his condition dirty. He received 75 grains/

grains more of Atoxyl in 25 injections and returned home improved. He was again seen in December 1914 and received two more injections and then ran away. His condition was very unsatisfactory and he apparently had not long to live. In March 1915 he was still alive at his home, but confined to his bed in the last stages of the disease.

Boyuku, female aged about 25. Was examined at her own request because her husband had sleeping sickness. She was found to be infected by gland puncture in Dec. 1911. ^{was treated with Atoxyl and} Symptoms were absent in her case. She/has remained healthy and married again. In March 1915 she gave birth to a healthy baby.

Embaba, aged 16, a house-boy to one of the missionaries. He was discovered to be infected with trypanosomes in October 1912. He had no symptoms at that time and was apparently in good health, but he had enlarged glands. He was treated with 15 injections of Atoxyl - grs. VI (90 grains in all) and six injections of $1\frac{1}{2}$ grains of tartar emetic into a vein of his arm. He remained well until January 1914. Then his whole moral character began to change. He became a thief and altogether untrustworthy. Soon after this which was the first sign that the disease was making progress, he became maniacal and died of exhaustion in July 1914.

Luka a boy aged 6 was brought by his parents because of headaches and fever and enlarged glands in November 1913. He was found to be infected and received a course of atoxyl. (75 grains in 25 injections). He made good progress at first, but only remained well for 9 or 10 months. The relapse showed itself suddenly by a slight epileptiform seizure. After this attack he became quickly weaker and did not wish to play with his friends. About the same time he was noticed to be suffering from a tendency to sleep in the daytime. His parents kept him clean, so he had not the usual neglected, dirty appearance of the Sleeping-sickness patient, but his tendency to sleep at all times was typical of the disease; also he had frequent high fevers and a rapid pulse and marked tremors. In the Autumn of 1914 (September) he had a series of severe epileptiform fits which lasted for 12 hours. Mustard baths would not control them. Bromide and chloral by rectum were tried without any result: Chloroform gave only temporary relief. Lumbar puncture, however, gave instant relief to the fits, but he was found to be suffering from hemiplegia when the fits had ceased. No trypanosomes were found in the spinal fluid (3ii) extracted, but the fluid was slightly turbid, and there were many mono-nuclear leucocytes on microscopical examination. He received 31 more injections of Atoxyl (grs.3) from October 1914 to January 1915, and improved slightly./

slightly. He was able to return to school in February 1915. In March 1915 he was still in the same condition and there had been no return of the fits. There are no signs of insanity, and his hemiplegia is improving, but the prognosis is, of course, of the gravest.

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